26. (New) A targeting construct comprising:

(a) a first polynucleotide sequence homologous to a first portion of a melanocyte stimulating hormone receptor gene;

(b) a second polynucleotide sequence homologous to second portion of a melanocyte stimulating hormone receptor gene; and

(c) a selectable marker located between the first polynucleotide sequence and the second polynucleotide sequence,

wherein the targeting construct when introduced into murine embryonic stem cells, results in a transgenic mouse having a disruption in a melanocyte stimulating hormone receptor gene, wherein the mouse when homozygous for a disruption in a melanocyte stimulating hormone receptor gene exhibits hypoactivity.

27. (New) The targeting construct of claim 26, wherein the targeting construct further comprises a screening marker, the screening marker positioned outside either the first polynucleotide sequence or the second polynucleotide sequence and opposite the selectable marker.

28. (New) A method of producing a targeting construct for a melanocyte stimulating hormone receptor gene, the method comprising:

(a) obtaining a first polynucleotide sequence homologous to a first region of a target gene;

(b) obtaining a second polynucleotide sequence homologous to a second region of a target gene;

(c) providing a vector comprising a selectable marker; and

(d) inserting the first and second sequences into the vector to produce the targeting construct,

wherein the targeting construct when introduced into murine embryonic stem cells, results in a transgenic mouse having a disruption in a melanocyte stimulating hormone receptor gene, wherein the mouse when homozygous for a disruption in a melanocyte stimulating hormone receptor gene exhibits hypoactivity.

29. (New) A method of producing a targeting construct for a melanocyte stimulating hormone receptor gene, the method comprising:

(a) providing a polynucleotide sequence homologous to a target gene;

(b) generating two different fragments of the polynucleotide sequence;

(c) providing a vector having a gene encoding a selectable marker; and

(d) inserting the two different fragments into the vector to form the targeting construct, wherein the targeting construct when introduced into murine embryonic stem cells results in a transgenic mouse having a disruption in a melanocyte stimulating hormone receptor gene, wherein the mouse when homozygous for a disruption in a melanocyte stimulating hormone receptor gene exhibits hypoactivity.

30. (New) A method of producing a transgenic mouse comprising a homozygous disruption in a melanocyte stimulating hormone receptor gene, the method comprising:

(a) introducing a melanocyte stimulating hormone receptor gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a homozygous disruption in a melanocyte stimulating hormone receptor gene, wherein the mouse when homozygous for a disruption in a melanocyte stimulating hormone receptor gene exhibits hypoactivity.

31. (New) A method of producing a transgenic mouse comprising a homozygous disruption in a melanocyte stimulating hormone receptor gene, the method comprising:

(a) providing a mouse embryonic stem cell comprising a disrupted melanocyte stimulating hormone receptor gene; and

(b) introducing the mouse embryonic stem cell into a pseudopregnant mouse, wherein

the pseudopregnant mouse gives birth to a chimeric mouse; and

(c) breeding the chimeric mouse to produce the transgenic mouse, wherein the mouse when homozygous for a disruption in a melanocyte stimulating hormone receptor gene exhibits hypoactivity.

32. (New) A transgenic mouse comprising a homozygous disruption in a melanocyte stimulating hormone receptor gene, wherein the transgenic mouse exhibits hypoactivity.

33. (New) A cell or tissue isolated from the transgenic mouse of claim 32.

34. (New) A transgenic mouse comprising a heterozygous disruption in a melanocyte stimulating hormone receptor gene, wherein said disruption in a homozygous state inhibits production of a functional melanocyte stimulating hormone receptor gene protein resulting in a transgenic mouse exhibiting hypoactivity.

35. (New) A cell transformed with the targeting construct of claim 26, wherein the cell comprises a disruption in a melanocyte stimulating hormone receptor gene.

REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 26-35 are pending after entry of the amendments set forth herein.

Claims 1-10 and 17-21 were examined. Claims 1-10 and 17-21 were rejected.

Please replace claims 1-10 and 17-21 with the clean version provided above.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

The newly added claims do not add new matter and are completely supported by the application as originally filed. More particularly, support for claims 26-29 directed to a targeting construct and methods of producing the targeting construct can be found, for example, at page